## SEQUENCE LISTING

```
RECEIVED
<110> Korpela, Matti
      Karp, Matti
                                                                       FEB 13 2001
      Kurittu, Jussi
                                                                     TECH CENTER 1600/2500
<120> A New Assay Method
<130> 2328-117
<140> US 09/529,967
<141> 2000-04-24
<150> PCT/FI98/00873
      1998-11-11
<151>
       FI 974235
<150>
       1997-11-14
<151>
       11
<160>
       PatentIn version 3.0
<170>
<210>
        1
        4846
<211>
<212>
       DNA
<213> Photinus pyralis
 <220>
 <221> misc_feature
 <222>
       (1) . (3098)
        /standard_name = "Vector pASK75"; /note= "Part of plasmid origina
        ting from vector pASK75; feature description below, SEQ ID 9-11."
 <223>
         /citation= ([2]
 <220>
 <221> CDS
        (3119)..(4768)
 <222>
        /product = "Photinus pyralis luciferase" /citation= ([1])
 <300>
 <302> Photinus pyralis luciferase: vectors that contain a modified luc
 coding sequence allowing convenient transfer into other systems
 <303>
        Gene
 <304>
        141
 <305>
        75-77
 <306>
        1994-04-08
 <307>
 <309>
        (3099)..(4772)
 <313>
 <300>
 <302> Use of the tetracycline promoter for the tightly regulated production
 of a murine antibody fragment in Escherichia coli
  <303>
         Gene
         151
  <304>
  <305>
         131-135
  <306>
  <307>
         1994-12-30
  <309>
         \overline{(1)..(3098)}
  <313>
```



agcttgacct gtgaagtgaa aaatggcgca cattgtgcga cattttttt gtctgccgtt 60 taccgctact gcgtcacgga tctccacgcg ccctgtagcg gcgcattaag cgcggcgggt 120 gtggtggtta cgcgcagcgt gaccgctaca cttgccagcg ccctagcgcc cgctcctttc 180 gctttcttcc cttcctttct cgccacgttc gccggctttc cccgtcaagc tctaaatcgg 240 gggctccctt tagggttccg atttagtgct ttacggcacc tcgaccccaa aaaacttgat 300 tagggtgatg gttcacgtag tgggccatcg ccctgataga cggtttttcg ccctttgacg 360 ttggagtcca cgttctttaa tagtggactc ttgttccaaa ctggaacaac actcaaccct 420 atctcggtct attcttttga tttataaggg attttgccga tttcggccta ttggttaaaa 480 aatgagctga tttaacaaaa atttaacgcg aattttaaca aaatattaac gcttacaatt 540 tcaggtggca cttttcgggg aaatgtgcgc ggaaccccta tttgtttatt tttctaaata 600 cattcaaata tgtatccgct catgagacaa taaccctgat aaatgcttca ataatattga 660 aaaaggaaga gtatgagtat tcaacatttc cgtgtcgccc ttattccctt ttttgcggca 720 ttttgccttc ctgtttttgc tcacccagaa acgctggtga aagtaaaaga tgctgaagat 780 cagttgggtg cacgagtggg ttacatcgaa ctggatctca acagcggtaa gatccttgag 840 900 agttttcgcc ccgaagaacg ttttccaatg atgagcactt ttaaagttct gctatgtggc geggtattat ecegtattga egeegggeaa gageaacteg gtegeegeat acaetattet 960 cagaatgact tggttgagta ctcaccagtc acagaaaagc atcttacgga tggcatgaca 1020 gtaagagaat tatgcagtgc tgccataacc atgagtgata acactgcggc caacttactt 1080 ctgacaacga tcggaggacc gaaggagcta accgcttttt tgcacaacat gggggatcat 1140 gtaactcgcc ttgatcgttg ggaaccggag ctgaatgaag ccataccaaa cgacgagcgt 1200 gacaccacga tgcctgtagc aatggcaaca acgttgcgca aactattaac tggcgaacta 1260 cttactctag cttcccggca acaattgata gactggatgg aggcggataa agttgcagga 1320 ccacttctgc gctcggccct tccggctggc tggtttattg ctgataaatc tggagccggt 1380 gagegtgget etegeggtat cattgeagea etggggeeag atggtaagee etecegtate 1440 gtagttatct acacgacggg gagtcaggca actatggatg aacgaaatag acagatcgct 1500 gagataggtg cctcactgat taagcattgg taggaattaa tgatgtctcg tttagataaa 1560 agtaaagtga ttaacagcgc attagagctg cttaatgagg tcggaatcga aggtttaaca 1620 acccgtaaac tcgcccagaa gctaggtgta gagcagccta cattgtattg gcatgtaaaa 1680 aataagcggg ctttgctcga cgccttagcc attgagatgt tagataggca ccatactcac 1740 ttttgccctt tagaagggga aagctggcaa gattttttac gtaataacgc taaaagtttt 1800 agatgtgctt tactaagtca tcgcgatgga gcaaaagtac atttaggtac acggcctaca 1860 gaaaaacagt atgaaactct cgaaaatcaa ttagcctttt tatgccaaca aggtttttca 1920

B

ctagagaatg cattatatgc actcagcgca gtggggcatt ttactttagg ttgcgtattg 1980 gaagatcaag agcatcaagt cgctaaagaa gaaagggaaa cacctactac tgatagtatg 2040 ccgccattat tacgacaagc tatcgaatta tttgatcacc aaggtgcaga gccagccttc 2100 ttattcggcc ttgaattgat catatgcgga ttagaaaaac aacttaaatg tgaaagtggg 2160 tcttaaaagc agcataacct ttttccgtga tggtaacttc actagtttaa aaggatctag 2220 gtgaagatcc tttttgataa tctcatgacc aaaatccctt aacgtgagtt ttcgttccac 2280 tgagcgtcag accccgtaga aaagatcaaa ggatcttctt gagatccttt ttttctgcgc 2340 gtaatctgct gcttgcaaac aaaaaaacca ccgctaccag cggtggtttg tttgccggat 2400 caagagctac caactetttt teegaaggta aetggettea geagagegea gataceaaat 2460 actgtccttc tagtgtagcc gtagttaggc caccacttca agaactctgt agcaccgcct 2520 acataceteg etetgetaat eetgttaeea gtggetgetg eeagtggega taagtegtgt 2580 cttaccgggt tggactcaag acgatagtta ccggataagg cgcagcggtc gggctgaacg 2640 gggggttcgt gcacacagcc cagcttggag cgaacgacct acaccgaact gagataccta 2700 cagegtgage tatgagaaag egecaegett eeegaaggga gaaaggegga eaggtateeg 2760 gtaagcggca gggtcggaac aggagagcgc acgagggagc ttccaggggg aaacgcctgg 2820 tatctttata gtcctgtcgg gtttcgccac ctctgacttg agcgtcgatt tttgtgatgc 2880 tcgtcagggg ggcggagcct atggaaaaac gccagcaacg cggccttttt acggttcctg 2940 gccttttgct ggccttttgc tcacatgacc cgacaccatc gaatggccag atgattaatt 3000 cctaattttt gttgacactc tatcattgat agagttattt taccactccc tatcagtgat 3060 agagaaaagt gaaatgaata gttcgacaaa aatctagaac tagtggatcc cccgtacc 3118 atg gaa gac gcc aaa aac ata aag aaa ggc ccg gcg cca ttc tat ccg 3166 Met Glu Asp Ala Lys Asn Ile Lys Lys Gly Pro Ala Pro Phe Tyr Pro cta gag gat gga acc gct gga gag caa ctg cat aag gct atg aag aga 3214 Leu Ğlu Asp Ğly Thr Ala Ğly Ğlu Gln Leu His Lys Ala Met Lys Arg tac gcc ctg gtt cct gga aca att gct ttt aca gat gca cat atc gag 3262 Tyr Ála Leu Val Pro Gly Thr Ile Ála Phe Thr Ásp Ála His Ile Glu 35 gtg aac atc acg tac gcg gaa tac ttc gaa atg tcc gtt cgg ttg gca 3310 Val Asn Ile Thr Tyr Ála Glu Tyr Phe Glu Met Ser Val Arg Leu Ala 55 50 gaa gct atg aaa cga tat ggg ctg aat aca aat cac aga atc gtc gta 3358 Glu Ala Met Lys Arg Tyr Gly Leu Asn Thr Asn His Arg Ile Val Val 65 tgc agt gaa aac tct ctt caa ttc ttt atg ccg gtg ttg ggc gcg tta 3406 Cys Ser Glu Asn Ser Leu Gln Phe Phe Met Pro Val Leu Gly Ala Leu 90 85



4	
ttt atc gga gtt gca gtt gcg ccc gcg aac gac att tat aat gaa cgt Phe Ile Gly Val Ala Val Ala Pro Ala Asn Asp Ile Tyr Asn Glu Arg 105	3454
gaa ttg ctc aac agt atg aac att tcg cag cct acc gta gtg ttt gtt Glu Leu Leu Asn Ser Met Asn Ile Ser Gln Pro Thr Val Val Phe Val 120 125	3502
tcc aaa aag ggg ttg caa aaa att ttg aac gtg caa aaa aaa tta cca Ser Lys Lys Gly Leu Gln Lys Ile Leu Asn Val Gln Lys Lys Leu Pro 135	3550
ata atc cag aaa att att atc atg gat tct aaa acg gat tac cag gga ata atc cag aaa att att atc atg gat tct aaa acg gat tac cag gga ata atc cag aaa att att atc atg gat tct aaa acg gat tac cag gga ata atc cag aaa att att atc atg gat tct aaa acg gat tac cag gga ata atc cag aaa att att atc atg gat tct aaa acg gat tac cag gga ata atc cag aaa att att atc atg gat tct aaa acg gat tac cag gga ata atc cag aaa att att atc atg gat tct aaa acg gat tac cag gga ata atc cag aaa att att atc atg gat tct aaa acg gat tac cag gga ata atc cag aaa att att atc atg gat tct aaa acg gat tac cag gga ata atc cag aaa att atc atc atg gat tct aaa acg gat tac cag gga atc atc atg gat tct aaa acg gat tac cag gga atc atc atg gat tct aaa acg gat tac cag gga atc atc atg gat tct aaa acg gat tac cag gga atc atc atg gat tct aaa acg gat tac cag gga atc atc atg gat tct aaa acg gat tac cag gga atc atc atg gat tct aaa acg gat tac cag gga atc atc atg gat tct aaa acg gat tac cag gga atc atc atg gat atc atc atg gat atc atc atg gat tct acc atg gat atc atc atc atc atc atc atc atc atc a	3598
145  ( ttt cag tcg atg tac acg ttc gtc aca tct cat cta cct ccc ggt ttt  Phe Gln Ser Met Tyr Thr Phe Val Thr Ser His Leu Pro Pro Gly Phe  165  170  175	3646
aat gaa tac gat ttt gta cca gag tcc ttt gat cgt gac aaa aca att Asn Glu Tyr Asp Phe Val Pro Glu Ser Phe Asp Arg Asp Lys Thr Ile 180 180	3694
gca ctg ata atg aac tcc tct gga tct act ggg tta cct aag ggt gtg Ala Leu Ile Met Asn Ser Ser Gly Ser Thr Gly Leu Pro Lys Gly Val 200 205	3742
gcc ctt ccg cat aga act gcc tgc gtc aga ttc tcg cat gcc aga gat Ala Leu Pro His Arg Thr Ala Cys Val Arg Phe Ser His Ala Arg Asp 215	3790
cct att ttt ggc aat caa atc att ccg gat act gcg att tta agt gtt Pro Ile Phe Gly Asn Gln Ile Ile Pro Asp Thr Ala Ile Leu Ser Val 230 240	3838
gtt cca ttc cat cac ggt ttt gga atg ttt act aca ctc gga tat ttg gtt pro Phe His His Gly Phe Gly Met Phe Thr Thr Leu Gly Tyr Leu Val Pro Phe His His Gly Phe Gly Met 250 255	3886
ata tgt gga ttt cga gtc gtc tta atg tat aga ttt gaa gaa gag ctg Ile Cys Gly Phe Arg Val Val Leu Met Tyr Arg Phe Glu Glu Leu 260 265	3934
ttt tta cga tcc ctt cag gat tac aaa att caa agt gcg ttg cta gta Phe Leu Arg Ser Leu Gln Asp Tyr Lys Ile Gln Ser Ala Leu Leu Val 285	3982
cca acc cta ttt tca ttc ttc gcc aaa agc act ctg att gac aaa tac Pro Thr Leu Phe Ser Phe Phe Ala Lys Ser Thr Leu Ile Asp Lys Tyr 290 295	4030
gat tta tct aat tta cac gaa att gct tct ggg ggc gca cct ctt tcg Asp Leu Ser Asn Leu His Glu Ile Ala Ser Gly Gly Ala Pro Leu Ser 310 315	4078
aaa gaa gtc ggg gaa gcg gtt gca aaa cgc ttc cat ctt cca ggg ata Lys Glu Val Gly Glu Ala Val Ala Lys Arg Phe His Leu Pro Gly Ile 335	
cga caa gga tat ggg ctc act gag act aca tca gct att ctg att aca Arg Gln Gly Tyr Gly Leu Thr Glu Thr Thr Ser Ala Ile Leu Ile Thr 340 345	4174



ob Carlo

ccc gag ggg gat gat aaa ccg ggc gcg gtc ggt aaa gtt gtt cca ttt 4222 Pro Glu Gly Asp Asp Lys Pro Gly Ala Val Gly Lys Val Val Pro Phe ttt gaa gcg aag gtt gtg gat ctg gat acc ggg aaa acg ctg ggc gtt 4270 Phe Glu Ala Lys Val Val Asp Leu Asp Thr Gly Lys Thr Leu Gly Val 375 370 aat cag aga ggc gaa tta tgt gtc aga gga cct atg att atg tcc ggt 4318 Asn Gln Arg Gly Glu Leu Cys Val Arg Gly Pro Met Ile Met Ser Gly 385 tat gta aac aat eeg gaa geg ace aac gee ttg att gae aag gat gga 4366 Tyr Val Asn Asn Pro Glu Ala Thr Asn Ala Leu Ile Asp Lys Asp Gly 405 tgg cta cat tct gga gac ata gct tac tgg gac gaa gac gaa cac ttc 4414 Trp Leu His Ser Gly Asp Ile Ala Tyr Trp Asp Glu Asp Glu His Phe 420 ttc ata gtt gac cgc ttg aag tct tta att aaa tac aaa gga tac cag 4462 Phe Ile Val Asp Arg Leu Lys Ser Leu Ile Lys Tyr Lys Gly Tyr Gln 435 gtg gcc ccc gct gaa ttg gag tcg ata ttg tta caa cac ccc aac atc 4510 Val Ala Pro Ala Glu Leu Glu Ser Ile Leu Leu Gln His Pro Asn Ile 450 ttc gac gcg ggc gtg gca ggt ctt ccc gac gat gac gcc ggt gaa ctt 4558 Phe Asp Ala Gly Val Ala Gly Leu Pro Asp Asp Asp Ala Gly Glu Leu 470 465 4606 ccc gcc gcc gtt gtt gtt ttg gag cac gga aag acg atg acg gaa aaa Pro Ala Ala Val Val Val Leu Glu His Gly Lys Thr Met Thr Glu Lys gag atc gtg gat tac gtc gcc agt caa gta aca acc gcc aaa aag ttg 4654 Glu Ile Val Asp Tyr Val Ala Ser Gln Val Thr Thr Ala Lys Lys Leu 500 cgc gga gga gtt gtg ttt gtg gac gaa gta ccg aaa ggt ctt acc gga 4702 Arg Gly Gly Val Val Phe Val Asp Glu Val Pro Lys Gly Leu Thr Gly aaa ctc gac gca aga aaa atc aga gag atc ctc ata aag gcc aag aag 4750 Lys Leu Asp Ala Arg Lys Ile Arg Glu Ile Leu Ile Lys Ala Lys Lys 4798 ggc gga aag tcc aaa ttg taaaatgtaa ctgtattcag cgatgacgaa Gly Gly Lys Ser Lys Leu 4846 attcttagct attgtaatac tctagcgggc tgcaggaatt cgatatca <210> 550 <211> PRT <212> <213> Photinus pyralis Met Glu Asp Ala Lys Asn Ile Lys Lys Gly Pro Ala Pro Phe Tyr Pro 1

8

: 4 G

Leu Glu Asp Gly Thr Ala Gly Glu Gln Leu His Lys Ala Met Lys Arg 20 25

Tyr Ala Leu Val Pro Gly Thr Ile Ala Phe Thr Asp Ala His Ile Glu 35

Val Asn Ile Thr Tyr Ala Glu Tyr Phe Glu Met Ser Val Arg Leu Ala 50 55

Glu Ala Met Lys Arg Tyr Gly Leu Asn Thr Asn His Arg Ile Val Val 65 70 80

Cys Ser Glu Asn Ser Leu Gln Phe Phe Met Pro Val Leu Gly Ala Leu 90 95

Phe Ile Gly Val Ala Val Ala Pro Ala Asn Asp Ile Tyr Asn Glu Arg 100 100

Glu Leu Leu Asn Ser Met Asn Ile Ser Gln Pro Thr Val Val Phe Val 115 120

Ser Lys Lys Gly Leu Gln Lys Ile Leu Asn Val Gln Lys Lys Leu Pro 130 135

Ile Ile Gln Lys Ile Ile Met Asp Ser Lys Thr Asp Tyr Gln Gly 145 150

Phe Gln Ser Met Tyr Thr Phe Val Thr Ser His Leu Pro Pro Gly Phe 170 175

Asn Glu Tyr Asp Phe Val Pro Glu Ser Phe Asp Arg Asp Lys Thr Ile 180

Ala Leu Ile Met Asn Ser Ser Gly Ser Thr Gly Leu Pro Lys Gly Val 195 200 205

Ala Leu Pro His Arg Thr Ala Cys Val Arg Phe Ser His Ala Arg Asp 210

Pro Ile Phe Gly Asn Gln Ile Ile Pro Asp Thr Ala Ile Leu Ser Val 225 230 240

Val Pro Phe His His Gly Phe Gly Met Phe Thr Thr Leu Gly Tyr Leu 255

Ile Cys Gly Phe Arg Val Val Leu Met Tyr Arg Phe Glu Glu Glu Leu 260 265

Phe Leu Arg Ser Leu Gln Asp Tyr Lys Ile Gln Ser Ala Leu Leu Val 275 280

Pro Thr Leu Phe Ser Phe Phe Ala Lys Ser Thr Leu Ile Asp Lys Tyr 290

Asp Leu Ser Asn Leu His Glu Ile Ala Ser Gly Gly Ala Pro Leu Ser 305

Lys Glu Val Gly Glu Ala Val Ala Lys Arg Phe His Leu Pro Gly Ile 335

Arg Gln Gly Tyr Gly Leu Thr Glu Thr Thr Ser Ala Ile Leu Ile Thr 340 340



. . .

t.

```
Pro Glu Gly Asp Asp Lys Pro Gly Ala Val Gly Lys Val Val Pro Phe
Phe Glu Ala Lys Val Val Asp Leu Asp Thr Gly Lys Thr Leu Gly Val
Asn Gln Arg Gly Glu Leu Cys Val Arg Gly Pro Met Ile Met Ser Gly
                     390
385
Tyr Val Asn Asn Pro Glu Ala Thr Asn Ala Leu Ile Asp Lys Asp Gly
Trp Leu His Ser Gly Asp Ile Ala Tyr Trp Asp Glu Asp Glu His Phe
 Phe Ile Val Asp Arg Leu Lys Ser Leu Ile Lys Tyr Lys Gly Tyr Gln
 Val Ala Pro Ala Glu Leu Glu Ser Ile Leu Leu Gln His Pro Asn Ile
                         455
     450
 Phe Asp Ala Gly Val Ala Gly Leu Pro Asp Asp Asp Ala Gly Glu Leu
 Pro Ala Ala Val Val Leu Glu His Gly Lys Thr Met Thr Glu Lys
 Glu Ile Val Asp Tyr Val Ala Ser Gln Val Thr Thr Ala Lys Lys Leu
  Arg Gly Gly Val Val Phe Val Asp Glu Val Pro Lys Gly Leu Thr Gly
  Lys Leu Asp Ala Arg Lys Ile Arg Glu Ile Leu Ile Lys Ala Lys Lys
  Gly Gly Lys Ser Lys Leu
   <210>
         10220
   <211>
   <212>
         DNA
         Photorhabdus luminescens
   <220>
          misc_feature
   <221>
          /standard_name= "vector pASK75" /note= "parts of plasmid originat
          (1)...(3190)
   <222>
          ing from vector pASK75" feature description below, SEQ ID NO:9-11
   <223>
          ." /citation= ([2]
   <220>
          misc_feature
   <221>
          /standard_name= "vector pASK75" /note= "parts of plasmid originat
    <222>
           ing from vector pASK75" feature description below, SEQ ID NO:9-11
           ." /citation= ([2]
    <220>
           CDS
    <221>
           (3634)..(5082)
    <222>
          /product= "Lux C" /citation= ([1])
```

u,t

```
<220>
<221>
      (5097)..(6017)
       /product= "Lux D" /citation= ([1])
<222>
<223>
<220>
       CDS
<221>
       (6069)..(7148)
<222>
       /product= "Lux A" /citation= ([1])
<223>
<220>
       CDS
<221>
        (7166) . . (8146)
        /product= "Lux B" /citation= ([1])
 <222>
 <223>
 <220>
 <221>
        CDS
        (8256)..(9437)
        /product= "Lux E" /citation= ([1])
 <222>
 <223>
 <300>
        Cloning, organization and expression of the bioluminescence genes of
 <301>
 <302>
 Xenorhabdus lumiminescenss
         J. Bacteriol.
  <303>
         172
  <304>
  <305>
         10
         5767-5773
  <306>
         1990-10-_
  <307>
  <309>
         (3191)..(10139)
  <313>
  <300>
         Use of the tetracycline promoter for the tightly regulated production
  <301>
  of a murine antibody fragment in Escherichia coli
         Gene
  <303>
          151
   <304>
   <305>
          131-135
   <306>
          1994-12-30
   <307>
          <u>(1).</u> (3190)
   <309>
   <313>
   agcttgacct gtgaagtgaa aaatggcgca cattgtgcga cattttttt gtctgccgtt
                                                                           60
   taccgctact gcgtcacgga tctccacgcg ccctgtagcg gcgcattaag cgcggcgggt
                                                                           120
   gtggtggtta cgcgcagcgt gaccgctaca cttgccagcg ccctagcgcc cgctcctttc
                                                                           180
    gctttcttcc cttcctttct cgccacgttc gccggctttc cccgtcaagc tctaaatcgg
                                                                           240
    gggctccctt tagggttccg atttagtgct ttacggcacc tcgaccccaa aaaacttgat
                                                                           300
    tagggtgatg gttcacgtag tgggccatcg ccctgataga cggtttttcg ccctttgacg
                                                                           360
    ttggagtcca cgttctttaa tagtggactc ttgttccaaa ctggaacaac actcaaccct
                                                                           420
    atctcggtct attcttttga tttataaggg attttgccga tttcggccta ttggttaaaa
                                                                           480
    aatgagctga tttaacaaaa atttaacgcg aattttaaca aaatattaac gcttacaatt
                                                                            540
     tcaggtggca cttttcgggg aaatgtgcgc ggaaccccta tttgtttatt tttctaaata
                                                                            600
```

cattcaaata tgtatccgct catgagacaa taaccctgat aaatgcttca ataatattga 660 aaaaggaaga gtatgagtat tcaacatttc cgtgtcgccc ttattccctt ttttgcggca 720 ttttgccttc ctgtttttgc tcacccagaa acgctggtga aagtaaaaga tgctgaagat 780 cagttgggtg cacgagtggg ttacatcgaa ctggatctca acagcggtaa gatccttgag 840 agttttcgcc ccgaagaacg ttttccaatg atgagcactt ttaaagttct gctatgtggc 900 gcggtattat cccgtattga cgccgggcaa gagcaactcg gtcgccgcat acactattct 960 cagaatgact tggttgagta ctcaccagtc acagaaaagc atcttacgga tggcatgaca 1020 gtaagagaat tatgcagtgc tgccataacc atgagtgata acactgcggc caacttactt 1080 ctgacaacga tcggaggacc gaaggagcta accgcttttt tgcacaacat gggggatcat 1140 gtaactcgcc ttgatcgttg ggaaccggag ctgaatgaag ccataccaaa cgacgagcgt 1200 gacaccacga tgcctgtagc aatggcaaca acgttgcgca aactattaac tggcgaacta 1260 cttactctag cttcccggca acaattgata gactggatgg aggcggataa agttgcagga 1320 ccacttctgc gctcggccct tccggctggc tggtttattg ctgataaatc tggagccggt 1380 gagcgtggct ctcgcggtat cattgcagca ctggggccag atggtaagcc ctcccgtatc 1440 gtagttatct acacgacggg gagtcaggca actatggatg aacgaaatag acagatcgct 1500 gagataggtg cctcactgat taagcattgg taggaattaa tgatgtctcg tttagataaa 1560 agtaaagtga ttaacagcgc attagagctg cttaatgagg tcggaatcga aggtttaaca 1620 accegtaaac tegeceagaa getaggtgta gageageeta eattgtattg geatgtaaaa 1680 aataagcggg ctttgctcga cgccttagcc attgagatgt tagataggca ccatactcac 1740 ttttgccctt tagaagggga aagctggcaa gattttttac gtaataacgc taaaagtttt 1800 agatgtgctt tactaagtca tcgcgatgga gcaaaagtac atttaggtac acggcctaca 1860 gaaaaacagt atgaaactct cgaaaatcaa ttagcctttt tatgccaaca aggtttttca 1920 1980 ctagagaatg cattatatgc actcagcgca gtggggcatt ttactttagg ttgcgtattg gaagatcaag agcatcaagt cgctaaagaa gaaagggaaa cacctactac tgatagtatg 2040 ccgccattat tacgacaagc tatcgaatta tttgatcacc aaggtgcaga gccagccttc 2100 ttattcggcc ttgaattgat catatgcgga ttagaaaaac aacttaaatg tgaaagtggg 2160 tcttaaaagc agcataacct ttttccgtga tggtaacttc actagtttaa aaggatctag 2220 gtgaagatcc tttttgataa tctcatgacc aaaatccctt aacgtgagtt ttcgttccac 2280 tgagcgtcag accccgtaga aaagatcaaa ggatcttctt gagatccttt ttttctgcgc 2340 gtaatctgct gcttgcaaac aaaaaaacca ccgctaccag cggtggtttg tttgccggat 2400 caagagctac caactetttt teegaaggta aetggettea geagagegea gataceaaat 2460 actgtccttc tagtgtagcc gtagttaggc caccacttca agaactctgt agcaccgcct 2520



w.

acataccteg ctctgctaat cctgttacca gtggctgctg ccagtggcga taagtcgtgt 2580 cttaccgggt tggactcaag acgatagtta ccggataagg cgcagcggtc gggctgaacg 2640 gggggttcgt gcacacagcc cagcttggag cgaacgacct acaccgaact gagataccta 2700 cagcgtgagc tatgagaaag cgccacgctt cccgaaggga gaaaggcgga caggtatccg 2760 gtaagcggca gggtcggaac aggagagcgc acgagggagc ttccaggggg aaacgcctgg 2820 tatctttata gtcctgtcgg gtttcgccac ctctgacttg agcgtcgatt tttgtgatgc 2880 togtcagggg ggcggagcct atggaaaaac gccagcaacg cggccttttt acggttcctg 2940 geettttget ggeettttge teacatgace egacaceate gaatggeeag atgattaatt 3000 cctaattttt gttgacactc tatcattgat agagttattt taccactccc tatcagtgat 3060 agagaaaagt gaaatgaata gttcgacaaa aatctagata acgagggcaa aaaatgaaaa 3120 agacagctat cgcgattgca gtggcactgg ctggtttcgc taccgtagcg caggcctgag 3180 accagaattc ttctttagaa atctgccggt aaaaattaga ttgctattca atctatttct 3240 atcggtattt gtgaaataat actcaggata ataatttaca taaatattat cacgcattag 3300 agaagagcat gactttttta atttaaactt ttcattaaca aatcttgttg atatgaaaat 3360 tttcctttgc tattttaaca gatattaaaa cgggaatagg cgttatattg acgatccatt 3420 cagttagatt aaaaaccttg agcagaaaat ttatattatt atcataatta tgacgaaagt 3480 tacaggccag gaaccacgta gtcagaatct gattttctat atatttgtta tttacatcgt 3540 cataacacaa aaatataaga agcaagtgtt ggtacgacca gttcgcaaga tagttaaaca 3600 gcaacttaag ttgaaattac ccccattaaa tgg atg gca aat atg act aaa aaa 3654 att tca ttc att att aac ggc cag gtt gaa atc ttt ccc gaa agt gat 3702 Ile Ser Phe Ile Ile Asn Gly Gln Val Glu Ile Phe Pro Glu Ser Asp gat tta gtg caa tcc att aat ttt ggt gat aat agt gtt tac ctg cca 3750 Asp Leu Val Gln Ser Ile Asn Phe Gly Asp Asn Ser Val Tyr Leu Pro 30 25 ata ttg aat gac tct cat gta aaa aac att att gat tgt aat gga aat 3798 Ile Leu Asn Ásp Ser His Val Lys Asn Ile Ile Ásp Cýs Asn Gly Asn aac gaa tta cgg ttg cat aac att gtc aat ttt ctc tat acg gta ggg 3846 Asn Glu Leu Arg Leu His Asn Ile Val Asn Phe Leu Tyr Thr Val Gly 60 caa aga tgg aaa aat gaa gaa tac tca aga cgc agg aca tac att cgt 3894 Gln Arg Trp Lys Asn Glu Glu Tyr Ser Arg Arg Arg Thr Tyr Ile Arg gac tta aaa aaa tat atg gga tat tca gaa gaa atg gct aag cta gag 3942 Ásp Leu Lys Lys Tyr Met Gly Tyr Ser Glu Glu Met Ála Lys Leu Glu 95



1.6

gcc aat tgg ata tct atg att tta tgt tct aaa ggc ggc ctt tat gat 3990 Ala Asn Trp Ile Ser Met Ile Leu Cys Ser Lys Gly Gly Leu Tyr Asp 105 gtt gta gaa aat gaa ctt ggt tct cgc cat atc atg gat gaa tgg cta 4038 Val Val Glu Asn Glu Leu Gly Ser Arg His Ile Met Ásp Glu Trp Leu 125 cct cag gat gaa agt tat gtt cgg gct ttt ccg aaa ggt aaa tct gta 4086 Pro Gln Asp Glu Ser Tyr Val Arg Ala Phe Pro Lys Gly Lys Ser Val 140 4134 cat ctg ttg gca ggt aat gtt cca tta tct ggg atc atg tct ata tta His Leu Leu Ála Gly Asn Val Pro Leu Ser Gly Ile Met Ser Ile Leu cgc gca att tta act aag aat cag tgt att ata aaa aca tcg tca acc 4182 Arg Ala Ile Leu Thr Lys Asn Gln Cys Ile Ile Lys Thr Ser Ser Thr 175 gat cct ttt acc gct aat gca tta gcg tta agt ttt att gat gta gac 4230 Asp Pro Phe Thr Ala Asn Ala Leu Ala Leu Ser Phe Ile Asp Val Asp 190 cct aat cat ccg ata acg cgc tct tta tct gtt ata tat tgg ccc cac 4278 Pro Asn His Pro Ile Thr Arg Ser Leu Ser Val Ile Tyr Trp Pro His 205 caa ggt gat aca tca ctc gca aaa gaa att atg cga cat gcg gat gtt 4326 Gln Gly Asp Thr Ser Leu Ala Lys Glu Ile Met Arg His Ala Asp Val att gtc gct tgg gga ggg cca gat gcg att aat tgg gcg gta gag cat 4374 Ile Val Ala Trp Gly Gly Pro Asp Ala Ile Asn Trp Ala Val Glu His gcg cca tct tat gct gat gtg att aaa ttt ggt tct aaa aag agt ctt 4422 Ala Pro Ser Tyr Ala Asp Val Ile Lys Phe Gly Ser Lys Lys Ser Leu tgc att atc gat aat cct gtt gat ttg acg tcc gca gcg aca ggt gcg 4470 Cys Ile Ile Asp Asn Pro Val Asp Leu Thr Ser Ala Ala Thr Gly Ala gct cat gat gtt tgt ttt tac gat cag cga gct tgt ttt tct gcc caa 4518 Ála His Ásp Val Cys Phe Tyr Ásp Gln Arg Ála Cys Phe Ser Ála Gln aac ata tat tac atg gga aat cat tat gag gaa ttt aag tta gcg ttg 4566 Asn Ile Tyr Tyr Met Gly Asn His Tyr Glu Glu Phe Lys Leu Ala Leu 300 ata gaa aaa ctt aat cta tat gcg cat ata tta ccg aat gcc aaa aaa 4614 Ile Glu Lys Leu Asn Leu Tyr Ala His Ile Leu Pro Asn Ala Lys Lys 315 gat ttt gat gaa aag gcg gcc tat tct tta gtt caa aaa gaa agc ttg 4662 Asp Phe Asp Glu Lys Ala Ala Tyr Ser Leu Val Gln Lys Glu Ser Leu 330 ttt gct gga tta aaa gta gag gtg gat att cat caa cgt tgg atg att 4710 Phe Ala Gly Leu Lys Val Glu Val Asp Ile His Gln Arg Trp Met Ile



بالربا المس

12	
att gag tca aat gca ggt gtg gaa ttt aat caa cca ctt ggc aga tgt Ile Glu Ser Asn Ala Gly Val Glu Phe Asn Gln Pro Leu Gly Arg Cys 375	4758
gtg tac ctt cat cac gtc gat aat att gag caa ata ttg cct tat gtt yal Tyr Leu His His Val Asp Asn Ile Glu Gln Ile Leu Pro Tyr Val 380 380	4806
caa aaa aat aag acg caa acc ata tct att ttt cct tgg gag tca tca Gln Lys Asn Lys Thr Gln Thr Ile Ser Ile Phe Pro Trp Glu Ser Ser	4854
395  ttt aaa tat cga gat gcg tta gca tta aaa ggt gcg gaa agg att gta  ttt aaa tat cga gat gcg tta gca tta aaa ggt gcg gaa agg att gta  Phe Lys Tyr Arg Asp Ala Leu Ala Leu Lys Gly Ala Glu Arg Ile Val  415  420	4902
gaa gca gga atg aat aac ata ttt cga gtt ggt gga tct cat gac gga Glu Ala Gly Met Asn Asn Ile Phe Arg Val Gly Gly Ser His Asp Gly	4950
atg aga ccg ttg caa cga tta gtg aca tat att tct cat gaa agg cca atg aga ccg ttg caa cga tta gtg aca tat att tct cat gaa agg cca  Met Arg Pro Leu Gln Arg Leu Val Thr Tyr Ile Ser His Glu Arg Pro  455	4998
440  440  440  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga  tct aac tat acg gct aag gat gtt gcg gtt gaa ata gaa cag act cga	5046
ttc ctg gaa gaa gat aag ttc ctt gta ttt gtc cca taataggtaa aagt Phe Leu Glu Glu Asp Lys Phe Leu Val Phe Val Pro 480	5096
atg gaa aat gaa tca aaa tat aaa acc atc gac cac gtt att tgt gtt atg gaa aat gaa tca aaa tat aaa acc atc gac cac gtt att tgt gtt atg gaa aat gaa tca aaa tat aaa acc atc gac cac gtt att tgt gtt atg gaa aat gaa tca aaa tat aaa acc atc gac cac gtt att tgt gtt	5144
gaa gga aat aaa aaa att cat gtt tgg gaa acg ctg cca gaa gaa aac gaa gga Bat aaa aaa att cat gtt tgg gaa acg ctg cca gaa gaa aac Glu Gly Asn Lys Lys Ile His Val Trp Glu Thr Leu Pro Glu Glu Asn	5192
agc cca aag aga aag aat gcc att att att gcg tct ggt ttt gcc cgc agc cca aag aga aag aat gcc att att att gcg tct ggt ttt gcc cgc agc cca aag aga aag aat gcc att att att gcg tct ggt ttt gcc cgc agc cca aag aga aag aat gcc att att att gcg tct ggt ttt gcc cgc agc cca aag aga aag aat gcc att att att gcg tct ggt ttt gcc cgc	5240
agg atg gat cat ttt gct ggt ctg gcg gaa tat tta tcg cgg aat gga Arg Met Asp His Phe Ala Gly Leu Ala Glu Tyr Leu Ser Arg Asn Gly	5288
ttt cat gtg atc cgc tat gat tcg ctt cac cac gtt gga ttg agt tca Phe His Val Ile Arg Tyr Asp Ser Leu His His Val Gly Leu Ser Ser	5336
ggg aca att gat gaa ttt aca atg tct ata gga aag cag agc ttg tta Gly Thr Ile Asp Glu Phe Thr Met Ser Ile Gly Lys Gln Ser Leu Leu 570 575	5384
gca gtg gtt gat tgg tta act aca cga aaa ata aat aac ttc ggt atg Ala Val Val Asp Trp Leu Thr Thr Arg Lys Ile Asn Asn Phe Gly Met 595	5432
ttg gct tca agc tta tct gcg cgg ata gct tat gca agc cta tct gaa ttg gct tca agc tta tct gcg cgg ata gct tat gca agc cta tct gaa Leu Ala Ser Ser Leu Ser Ala Arg Ile Ala Tyr Ala Ser Leu Ser Glu 605 610	5480



556	28
atc aat gct tcg ttt tta atc acc gca gtc ggt gtt gtt aac tta aga 55%  Ile Asn Ala Ser Phe Leu Ile Thr Ala Val Gly Val Val Asn Leu Arg 625 620 625	
	576
6 <del>4</del> (1	624
gaa gtc ttt gcg aga gat tgt ctt gat ttt ggt tgg gaa gat tta gct 50 Glu Val Phe Ala Arg Asp Cys Leu Asp Phe Gly Trp Glu Asp Leu Ala 675	672
660  tct aca att aat aac atg atg tat ctt gat ata ccg ttt att gct ttt  tct aca att aat aac atg atg tat ctt gat ata ccg ttt att gct ttt  Ser Thr Ile Asn Asn Met Met Tyr Leu Asp Ile Pro Phe Ile Ala Phe  685  685	5720
act gca aat aac gat aat tgg gtc aag caa gat gaa gtt atc aca ttg act gca aat aac gat aat tgg gtc aag caa gat gaa gtt atc aca ttg act gca aat aac gat aat tgg gtc aag caa gat gaa gtt atc aca ttg act gca act gca aat aac gat aat tgg gtc aag caa gat gaa gtt atc aca ttg act gca act gc	5768
tta tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tta tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tta tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tta tca aat att cgt agt agt cga tgc aag ata tat tct ttg tta gga tta tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tta tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tta tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tta tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tta tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tca tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tca tca aat att cgt agt aat cga tgc aag ata tat tct ttg tta gga tca tca aat att cgt agt agt aat cga tgc aag ata tat tct ttg tta gga tca tca act att cgt agt agt agt agt agt agt agt agt agt a	5816
	5864
caa tog gtt acg aaa gcc gct atc gcg atg gat aat gat cat ctg gat cas tog gtt acg aaa gcc gct atc gcg atg gat aat gat cat ctg gat can tog gtt acg aaa gcc gct atc gcg atg gat aat gat cat ctg gat can tog gtt acg aaa gcc gct atc gcg atg gat aat gat cat ctg gat can tog gtt acg aaa gcc gct atc gcg atg gat aat gat cat ctg gat	5912
740  att gat gtt gat att act gaa ccg tca ttt gaa cat tta act att gcg att gat gtt gat att act gaa ccg tca ttt gaa cat tta act att gcg att gat gtt gat att act gaa ccg tca ttt gaa cat tta act att gcg att gat gtt gat att act gaa ccg tca ttt gaa cat tta act att gcg att gat gtt gat att act gaa ccg tca ttt gaa cat tta act att gcg att gat gtt gat att act gcg	5960
aca gtc aat gaa cgc cga atg aga att gag att gaa aat caa gca att arg Ile Glu Ile Glu Asn Gln Ala Ile Thr Val Asn Glu Arg Arg Met Arg Ile Glu Ile Glu Asn 785	6008
tct ctg tct taaaatctat tgagatattc tatcactcaa atagcaatat Ser Leu Ser	6057
790  aaggactctc t atg aaa ttt gga aac ttt ttg ctt aca tac caa cct ccc aaggactctc t atg aaa ttt gga aac ttt ttg ctt aca tac caa cct ccc  Met Lys Phe Gly Asn Phe Leu Leu Thr Tyr Gln Pro Pro  795	6107
caa ttt tct caa aca gag gta atg aaa cgt ttg gtt aaa tta ggt cgc Gln Phe Ser Gln Thr Glu Val Met Lys Arg Leu Val Lys Leu Gly Arg 810	6155
atc tct gag gag tgt ggt ttt gat acc gta tgg tta ctg gag cat cat  atc tct gag gag tgt ggt ttt gat acc gta tgg tta ctg gag cat cat  Ile Ser Glu Glu Cys Gly Phe Asp Thr Val Trp Leu Leu Glu His His  835  835	6203
820  ttc acg gag ttt ggt ttg ctt ggt aac cct tat gtc gct gct gca tat  ttc acg gag ttt ggt ttg ctt ggt aac cct tat gtc gct gca tat  Phe Thr Glu Phe Gly Leu Leu Gly Asn Pro Tyr Val Ala Ala Ala Tyr  840  840	6251

or w.

14	
tta ctt ggc gcg act aaa aaa ttg aat gta gga act gcc gct att gtt Leu Leu Gly Ala Thr Lys Lys Leu Asn Val Gly Thr Ala Ala Ile Val 855	6299
ctt ccc aca gcc cat cca gta cgc caa ctt gaa gat gtg aat tta ttg Leu Pro Thr Ala His Pro Val Arg Gln Leu Glu Asp Val Asn Leu Leu 875	6347
gat caa atg tca aaa gga cga ttt cgg ttt ggt att tgc cga ggg ctt Asp Gln Met Ser Lys Gly Arg Phe Arg Phe Gly Ile Cys Arg Gly Leu 890 895	6395
tac aac aag gac ttt cgc gta ttc ggc aca gat atg aat aac agt cgc  Tyr Asn Lys Asp Phe Arg Val Phe Gly Thr Asp Met Asn Asn Ser Arg  915	6443
gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg tac ggg ctg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg ata aag aat ggc atg aca gag  gcc tta gcg gaa tgc tgg ata aag aat ggc atg aca gag  all tac gcg gaa tgc tgg ata aag aat ggc atg aca gag  all tac gcg gaa tgc tgg ata aag aat ggc atg aca gag  all tac gcg gaa tgc gag aca gag ac	6491
gga tat atg gaa gct gat aat gaa cat atc aag ttc cat aag gta aaa Gly Tyr Met Glu Ala Asp Asn Glu His Ile Lys Phe His Lys Val Lys 945 935	6539
gta aac ccc gcg gcg tat agc aga ggt ggc gca ccg gtt tat gtg gtg Val Asn Pro Ala Ala Tyr Ser Arg Gly Gly Ala Pro Val Tyr Val Val 955	6587
gct gaa tca gct tcg acg act gag tgg gct gct caa ttt ggc cta ccg gct gaa tca gct tcg acg act gag tgg gct gct caa ttt ggc cta ccg Ala Glu Ser Ala Ser Thr Thr Glu Trp Ala Ala Gln Phe Gly Leu Pro 970 975	6635
atg ata tta agt tgg att ata aat act aac gaa aag aaa gca caa ctt  atg ata tta agt tgg att ata aat act aac gaa aag aaa gca caa ctt  Met Ile Leu Ser Trp Ile Ile Asn Thr Asn Glu Lys Lys Ala Gln Leu  995  985	6683
980  gag ctt tat aat gaa gtg gct caa gaa tat ggg cac gat att cat  gag ctt tat aat gaa gtg gct caa gaa tat ggg cac gat att cat  Glu Leu Tyr Asn Glu Val Ala Gln Glu Tyr Gly His Asp Ile His  Glu Leu Tyr Asn Glu Val Ala Gln Glu Tyr 1005	6728
aat atc gac cat tgc tta tca tat ata aca tct gta gat cat gac Asn Ile Asp His Cys Leu Ser Tyr Ile Thr Ser Val Asp His Asp 1025 1015	6773
tca att aaa gcg aaa gag att tgc cgg aaa ttt ctg ggg cat tgg  tca att aaa gcg aaa gag att tgc cgg aaa ttt ctg ggg cat tgg  Ser Ile Lys Ala Lys Glu Ile Cys Arg Lys Phe Leu Gly His Trp  1040  1030	6818
tat gat tct tat gtg aat gct acg act att ttt gat gat tca gac tat gat tct tat gtg aat gct acg act att ttt gat gat tca gac Tyr Asp Ser Tyr Val Asn Ala Thr Thr Ile Phe Asp Asp Ser Asp 1050 1055	6863
caa aca aga ggt tat gat ttc aat aaa ggg cag tgg cgt gac ttt Gln Thr Arg Gly Tyr Asp Phe Asn Lys Gly Gln Trp Arg Asp Phe 1065	6908
1060  gta tta aaa gga cat aaa gat act aat cgc cgt att gat tac agt  gta tta aaa gga cat aaa gat act aat cgc cgt att gat tac agt  Val Leu Lys Gly His Lys Asp Thr Asn Arg Arg Ile Asp Tyr Ser  1085	6953
tac gaa atc aat ccc gtg gga acg ccg cag gaa tgt att gac ata Tyr Glu Ile Asn Pro Val Gly Thr Pro Gln Glu Cys Ile Asp Ile 1090 1090	6998



 $\phi_{ij} = \phi_{ij}$ 

att caa aaa gac att gat gct aca gga ata tca aat att tgt tgt Ile Gln Lys Asp Ile Asp Ala Thr Gly Ile Ser Asn Ile Cys Cys 7043 1105 gga ttt gaa gct aat gga aca gta gac gaa att att gct tcc atg Gly Phe Glu Ala Asn Gly Thr Val Asp Glu Ile Ile Ala Ser Met 7088 1120 aag ctc ttc cag tct gat gtc atg cca ttt ctt aaa gaa aaa caa Lys Leu Phe Gln Ser Asp Val Met Pro Phe Leu Lys Glu Lys Gln 7133 cgt tcg cta tta tat tagctaagga gaaagaa atg aaa ttt gga ttg ttc 7183 Met Lys Phe Gly Leu Phe Arg Ser Leu Leu Tyr 1150 ttc ctt aac ttc atc aat tca aca act gtt caa gaa caa agt ata Phe Leu Asn Phe Ile Asn Ser Thr Thr Val Gln Glu Gln Ser Ile 7228 1160 gtt cgc atg cag gaa ata acg gag tat gtt gat aag ttg aat ttt Val Arg Met Gln Glu Ile Thr Glu Tyr Val Asp Lys Leu Asn Phe 7273 1175 gaa cag att tta gtg tat gaa aat cat ttt tca gat aat ggt gtt Glu Gln Ile Leu Val Tyr Glu Asn His Phe Ser Asp Asn Gly Val 7318 1190 gtc ggc gct cct ctg act gtt tct ggt ttt ctg ctc ggt tta Val Gly Ala Pro Leu Thr Val Ser Gly Phe Leu Leu Gly Leu 7363 aca 1205 gag aaa att aaa att ggt toa tta aat cac atc att aca act Glu Lys Ile Lys Ile Gly Ser Leu Asn His Ile Ile Thr Thr 7408 cat His cat cct gtc gcc ata gcg gag gaa gct tgc tta ttg gat cag tta His Pro Val Ala Ile Ala Glu Glu Ala Cys Leu Leu Asp Gln Leu 7453 1235 agt gaa ggg aga ttt att tta ggg ttt agt gat tgc gaa aaa aaa 7498 Ser Glu Gly Arg Phe Ile Leu Gly Phe Ser Asp Cys Glu Lys gat gaa atg cat ttt ttt aat cgc ccg gtt gaa tat caa cag caa Asp Glu Met His Phe Phe Asn Arg Pro Val Glu Tyr Gln Gln Gln 7543 cta ttt gaa gag tgt tat gaa atc att aac gat gct tta aca Leu Phe Glu Glu Cys Tyr Glu Ile Ile Asn Asp Ala Leu Thr 7588 aca 1280 ggc tat tgt aat cca gat aac gat ttt tat agc ttc cct aaa Gly Tyr Cys Asn Pro Asp Asn Asp Phe Tyr Ser Phe Pro Lys 7633 1295 tct gta aat ccc cat gct tat acg cca ggc gga cct cgg aaa Ser Val Asn Pro His Ala Tyr Thr Pro Gly Gly Pro Arg Lys 7678 tat Tyr gta aca gca acc agt cat cat att gtt gag tgg gcg gcc aaa aaa Val Thr Ala Thr Ser His His Ile Val Glu Trp Ala Ala Lys Lys 7723 1325



te ny

16	
ggt att cct ctc atc ttt aag tgg gat gat tct aat gat gtt aga 7 Gly Ile Pro Leu Ile Phe Lys Trp Asp Asp Ser Asn Asp Val Arg 1340 1340	768
tat gaa tat gct gaa aga tat aaa gcc gtt gcg gat aaa tat gac  tat gaa tat gct gaa aga tat aaa gcc gtt gcg gat aaa tat gac  Tyr Glu Tyr Ala Glu Arg Tyr Lys Ala Val Ala Asp Lys Tyr Asp  1365  1355	7813
gtt gac cta tca gag ata gac cat cag tta atg ata tta gtt aac gtt gac cta tca gag ata gac cat cag tta atg ata tta gtt aac Val Asp Leu Ser Glu Ile Asp His Gln Leu Met Ile Leu Val Asn 1370 1370	7858
tat aac gaa gat agt aat aaa gct aaa caa gag acg cgt gca ttt  tat aac gaa gat agt aat aaa gct aaa caa gag acg cgt gca ttt  Tyr Asn Glu Asp Ser Asn Lys Ala Lys Gln Glu Thr Arg Ala Phe  1395  1385	7903
att agt gat tat gtt ctt gaa atg cac cct aat gaa aat ttc gaa att agt gat tat gtt ctt gaa atg cac cct aat gaa aat ttc gaa Ile Ser Asp Tyr Val Leu Glu Met His Pro Asn Glu Asn Phe Glu 1400 1400	7948
aat aaa ctt gaa gaa ata att gca gaa aac gct gtc gga aat tat Asn Lys Leu Glu Glu Ile Ile Ala Glu Asn Ala Val Gly Asn Tyr 1425	7993
acg gag tgt ata act gcg gct aag ttg gca att gaa aag tgt ggt  acg gag tgt ata act gcg gct aag ttg gca att gaa aag tgt ggt  Thr Glu Cys Ile Thr Ala Ala Lys Leu Ala Ile Glu Lys Cys Gly  1435	8038
gcg aaa agt gta ttg ctg tcc ttt gaa cca atg aat gat ttg atg Ala Lys Ser Val Leu Leu Ser Phe Glu Pro Met Asn Asp Leu Met 1450	8083
agc caa aaa aat gta atc aat att gtt gat gat aat att aag aag agc caa aaa aat gta atc aat att gtt gat gat aat att aag aag Ser Gln Lys Asn Val Ile Asn Ile Val Asp Asp Asn Ile Lys Lys 1465	8128
tac cac atg gaa tat acc taatagattt cgagttgcag cgaggcggca Tyr His Met Glu Tyr Thr	8176
1475  agtgaacgaa tccccaggag catagataac tatgtgactg gggtgagtga aagcagccaa	8236
agtgaacgaa tccccaygay cutayer caaagcagca gcttgaaag atg aag ggt ata aaa gag tat gac agc agt caaagcagca gcttgaaag atg aag ggt ata aaa gag tat gac agc Met Lys Gly Ile Lys Glu Tyr Asp Ser Ser 1480	8285
gct gcc ata ctt tct aat att atc ttg agg agt aaa aca ggt atg Ala Ala Ile Leu Ser Asn Ile Ile Leu Arg Ser Lys Thr Gly Met 1495	8330
act tca tat gtt gat aaa caa gaa att aca gca agc tca gaa att  Thr Ser Tyr Val Asp Lys Gln Glu Ile Thr Ala Ser Ser Glu Ile  1515 1505	8375
gat gat ttg att ttt tcg agc gat cca tta gtg tgg tct tac gac gat gat ttg att ttt tcg agc gat cca tta gtg tgg tct tac gac Asp Asp Leu Ile Phe Ser Ser Asp Pro Leu Val Trp Ser Tyr Asp 1530 1520	8420
gag cag gaa aaa atc aga aag aaa ctt gtg ctt gat gca ttt cgt gag cag gaa aaa atc aga aag aaa ctt gtg ctt gat gca ttt cgt Leu Asp Ala Phe Arg Glu Gln Glu Lys Ile Arg Lys Lys Leu Val Leu Asp Ala Phe Arg 1545 1535	8465



 $\mathcal{S}^{\alpha}_{-\alpha} = \mathcal{S}^{\alpha}_{-\alpha}$ 

17	
aat cat tat aaa cat tgt cga gaa tat cgt cac tac tgt cag gca Asn His Tyr Lys His Cys Arg Glu Tyr Arg His Tyr Cys Gln Ala 1550 1555	8510
cac aaa gta gat gac aat att acg gaa att gat gac ata cct gta His Lys Val Asp Asp Asn Ile Thr Glu Ile Asp Asp Ile Pro Val 1570	8555
ttc cca aca tcg gtt ttt aag ttt act cgc tta tta act tct cag ttc cca aca tcg gtt ttt aag ttt Arg Leu Leu Thr Ser Gln Phe Pro Thr Ser Val Phe Lys Phe Thr Arg Leu Leu Thr Ser Gln 1585	8600
gaa aac gag att gaa agt tgg ttt acc agt agc ggc acg aat ggt Glu Asn Glu Ile Glu Ser Trp Phe Thr Ser Ser Gly Thr Asn Gly	8645
tta aaa agt cag gtg gcg cgt gac aga tta agt att gag aga ctc Leu Lys Ser Gln Val Ala Arg Asp Arg Leu Ser Ile Glu Arg Leu 1615	8690
tta ggc tct gtg agt tat ggc atg aaa tat gtt ggt agt tgg ttt  tta ggc tct gtg agt tat ggc atg aaa tat gtt ggt agt tgg ttt  Leu Gly Ser Val Ser Tyr Gly Met Lys Tyr Val Gly Ser Trp Phe  1630 1635	8735
gat cat caa ata gaa tta gtc aat ttg gga cca gat aga ttt aat gat cat caa ata gaa tta gtc aat ttg gga cca gat aga ttt aat gat cat caa ata gaa tta gtc aat ttg gga cca gat aga ttt aat gat cat caa ata gaa tta gtc aat ttg gga cca gat aga ttt aat	8780
gct cat aat att tgg ttt aaa tat gtt atg agt ttg gtg g	8825
1655  tta tat cct acg aca ttt acc gta aca gaa gaa cga ata gat ttt  tta tat cct acg aca ttt acc gta Thr Glu Glu Arg Ile Asp Phe	8870
1670  1670  1670  gtt aaa aca ttg aat agt ctt gaa cga ata aaa aat caa ggg aaa  gtt aaa aca ttg aat agt ctt gaa leu Arg Ile Lys Asn Gln Gly Lys	8915
gat ctt tgt ctt att ggt tcg cca tac ttt att tat tta ctc tgc gat ctt tgt ctt att ggt tcg cca Tyr Phe Ile Tyr Leu Leu Cys	8960
1700  1700  1700  cat tat atg aaa gat aaa aaa atc tca ttt tct gga gat aaa agc  cat tat atg aaa gat aaa aaa atc tca ttt tct gga gat aaa agc  cat tat atg Ser Bur Met Lys Asp Lys Lys Ile Ser Phe Ser Gly Asp Lys Ser	9005
ctt tat atc ata acc gga ggc ggc tgg aaa agt tac gaa aaa gaa	9050
tct ctg aaa cgt gat gat ttc aat cat ctt tta ttt gat act ttc  tct ctg aaa cgt gat gat ttc aat cat ctt tta ttt gat act ttc	9095
aat ctc agt gat att agt cag atc cga gat ata ttt aat caa gtt aat ctc agt gat att agt cag atc Asp Ile Phe Asn Gln Val	9140
gaa ctc aac act tgt ttc ttt gag gat gaa atg cag cgt aaa cat Glu Leu Asn Thr Cys Phe Phe Glu Asp Glu Met Gln Arg Lys His 1785	9185

 $v^{\alpha}$  ,  $v^{\alpha}$ 

gtt ccg ccg tgg gta tat gcg cga gcg ctt gat cct gaa acg ttg Val Pro Pro Trp Val Tyr Ala Arg Ala Leu Asp Pro Glu Thr Leu 9230 1790 aaa cct gta cct gat gga acg ccg ggg ttg atg agt tat Lys Pro Val Pro Asp Gly Thr Pro Gly Leu Met Ser Tyr 9275 atg gat Met Asp 1810 1805 gcg tca gca acc agt tat cca gca ttt att gtt acc gat Ala Ser Ala Thr Ser Tyr Pro Ala Phe Ile Val Thr Asp 9320 gat gtc Asp Val Phe Ile Val Thr Asp 1820 agc aga gaa tat ggt aag tat ccc ggc gtg ctc gtt 9365 Gly Ile Ile Ser Arg Glu Tyr Gly Lys Tyr Pro Gly Val 1840 9410 cgt cgc gtc aat acg agg acg cag aaa ggg tgt gct Arg Arg Val Asn Thr Arg Thr Gln Lys Gly Cys Ala gaa att tta Glu Ile Leu 1855 1850 acc gaa gcg ttt gat agt tgatatcctt tgcctaattg 9457 tta agc tta Thr Glu Ala Phe Asp Ser Leu Ser Leu 1870 1865 taagtggaat gcttgcgtta tataaatctg aatgacatct acactttaca aaattctcca 9517 aaacatccac atttgggtac ttgatagagg tttatggggt tggcttaaca ttgttctcat 9577 tgttattatt ggctcaaagc aaaaggagat aacatgaaaa aattggcagt tatgcttgca 9637 ttgggaatga ttagctttgg tgcaatggca gttgatgggt ataaagatgc aaagtttggc 9697 atgacagaag aagagtttct ttcgaagagg ttatgtgatt ttgaaaaatt tgagggagat 9757 tetegaatag aagaagtate aetttattea tgttetgaet tttegtttge taacaaaaag 9817 cgtgaagcaa tggcattttt tttaaatggg aaatttaaaa gattagagat taatattggc 9877 agacttgtga agccagtaag caaatcgtta acgaaaaagt acggagatgg atcatcgtat 9937 ccatcaaaag aagaatttga gaacgcgcta aaatacaatg gaactatgtc tataggttat 9997 gataataata cggtattagt tgatatacat ataatatgtg gcaaagaagg catagaaacc 10057 agtcaactga tttatacgag tccagatgtt tatacgctcc cagatttcgg agaaaaaatc 10117 caggaattaa agggattaaa ggaattcgag ctcggtaccc ggggatccct cgaggtcgac 10177 10220 ctgcaggcag cgcttggcgt cacccgcagt tcggtggtta ata 4 <210> 483 <211> <212> PRT Photorhabdus luminescens <213>

Met Ala Asn Met Thr Lys Lys Ile Ser Phe Ile Ile Asn Gly Gln Val 1 10 15

Glu Ile Phe Pro Glu Ser Asp Asp Leu Val Gln Ser Ile Asn Phe Gly 20

Asp Asn Ser Val Tyr Leu Pro Ile Leu Asn Asp Ser His Val Lys Asn 35

Ile Ile Asp Cys Asn Gly Asn Asn Glu Leu Arg Leu His Asn Ile Val 50 55

Asn Phe Leu Tyr Thr Val Gly Gln Arg Trp Lys Asn Glu Glu Tyr Ser 75 80

Arg Arg Arg Thr Tyr Ile Arg Asp Leu Lys Lys Tyr Met Gly Tyr Ser 85 90

Glu Glu Met Ala Lys Leu Glu Ala Asn Trp Ile Ser Met Ile Leu Cys 100 100

Ser Lys Gly Gly Leu Tyr Asp Val Val Glu Asn Glu Leu Gly Ser Arg 115 120 125

His Ile Met Asp Glu Trp Leu Pro Gln Asp Glu Ser Tyr Val Arg Ala 130 135

Phe Pro Lys Gly Lys Ser Val His Leu Leu Ala Gly Asn Val Pro Leu 145 150 150

Ser Gly Ile Met Ser Ile Leu Arg Ala Ile Leu Thr Lys Asn Gln Cys 165 170 175

Ile Ile Lys Thr Ser Ser Thr Asp Pro Phe Thr Ala Asn Ala Leu Ala 180 185

Leu Ser Phe Ile Asp Val Asp Pro Asn His Pro Ile Thr Arg Ser Leu 195 200 205

Ser Val Ile Tyr Trp Pro His Gln Gly Asp Thr Ser Leu Ala Lys Glu 210

Ile Met Arg His Ala Asp Val Ile Val Ala Trp Gly Gly Pro Asp Ala 225 230 230

Ile Asn Trp Ala Val Glu His Ala Pro Ser Tyr Ala Asp Val Ile Lys 255

Phe Gly Ser Lys Lys Ser Leu Cys Ile Ile Asp Asn Pro Val Asp Leu 260 265 270

Thr Ser Ala Ala Thr Gly Ala Ala His Asp Val Cys Phe Tyr Asp Gln 275

Arg Ala Cys Phe Ser Ala Gln Asn Ile Tyr Tyr Met Gly Asn His Tyr 290 295

Glu Glu Phe Lys Leu Ala Leu Ile Glu Lys Leu Asn Leu Tyr Ala His 305

Ile Leu Pro Asn Ala Lys Lys Asp Phe Asp Glu Lys Ala Ala Tyr Ser 325

Leu Val Gln Lys Glu Ser Leu Phe Ala Gly Leu Lys Val Glu Val Asp 340 345

Ile His Gln Arg Trp Met Ile Ile Glu Ser Asn Ala Gly Val Glu Phe 355



1 (1) Ell's

Asn Gln Pro Leu Gly Arg Cys Val Tyr Leu His His Val Asp Asn Ile

Glu Gln Ile Leu Pro Tyr Val Gln Lys Asn Lys Thr Gln Thr Ile Ser

Ile Phe Pro Trp Glu Ser Ser Phe Lys Tyr Arg Asp Ala Leu Ala Leu

Lys Gly Ala Glu Arg Ile Val Glu Ala Gly Met Asn Asn Ile Phe Arg

Val Gly Gly Ser His Asp Gly Met Arg Pro Leu Gln Arg Leu Val Thr

Tyr Ile Ser His Glu Arg Pro Ser Asn Tyr Thr Ala Lys Asp Val Ala

Val Glu Ile Glu Gln Thr Arg Phe Leu Glu Glu Asp Lys Phe Leu Val

Phe Val Pro

<210>

307 <211>

<212> PRT

<213> Photorhabdus luminescens

Met Glu Asn Glu Ser Lys Tyr Lys Thr Ile Asp His Val Ile Cys Val

Glu Gly Asn Lys Lys Ile His Val Trp Glu Thr Leu Pro Glu Glu Asn 25

Ser Pro Lys Arg Lys Asn Ala Ile Ile Ile Ala Ser Gly Phe Ala Arg 35 40

Arg Met Asp His Phe Ala Gly Leu Ala Glu Tyr Leu Ser Arg Asn Gly

Phe His Val Ile Arg Tyr Asp Ser Leu His His Val Gly Leu Ser Ser 65 70 75

Gly Thr Ile Asp Glu Phe Thr Met Ser Ile Gly Lys Gln Ser Leu Leu

Ala Val Val Asp Trp Leu Thr Thr Arg Lys Ile Asn Asn Phe Gly Met

Leu Ala Ser Ser Leu Ser Ala Arg Ile Ala Tyr Ala Ser Leu Ser Glu

Ile Asn Ala Ser Phe Leu Ile Thr Ala Val Gly Val Val Asn Leu Arg 135

Tyr Ser Leu Glu Arg Ala Leu Gly Phe Asp Tyr Leu Ser Leu Pro Ile

Asn Glu Leu Pro Asp Asn Leu Asp Phe Glu Gly His Lys Leu Gly Ala

Glu Val Phe Ala Arg Asp Cys Leu Asp Phe Gly Trp Glu Asp Leu Ala

Ser Thr Ile Asn Asn Met Met Tyr Leu Asp Ile Pro Phe Ile Ala Phe

Thr Ala Asn Asn Asp Asn Trp Val Lys Gln Asp Glu Val Ile Thr Leu

Leu Ser Asn Ile Arg Ser Asn Arg Cys Lys Ile Tyr Ser Leu Leu Gly

Ser Ser His Asp Leu Ser Glu Asn Leu Val Val Leu Arg Asn Phe Tyr

Gln Ser Val Thr Lys Ala Ala Ile Ala Met Asp Asn Asp His Leu Asp 260

Ile Asp Val Asp Ile Thr Glu Pro Ser Phe Glu His Leu Thr Ile Ala

Thr Val Asn Glu Arg Arg Met Arg Ile Glu Ile Glu Asn Gln Ala Ile

Ser Leu Ser 305

<210>

360 <211>

PRT <212>

<213> Photorhabdus luminescens

Met Lys Phe Gly Asn Phe Leu Leu Thr Tyr Gln Pro Pro Gln Phe Ser 10 15

Gln Thr Glu Val Met Lys Arg Leu Val Lys Leu Gly Arg Ile Ser Glu

Glu Cys Gly Phe Asp Thr Val Trp Leu Leu Glu His His Phe Thr Glu

Phe Gly Leu Leu Gly Asn Pro Tyr Val Ala Ala Ala Tyr Leu Leu Gly

Ala Thr Lys Lys Leu Asn Val Gly Thr Ala Ala Ile Val Leu Pro Thr

Ala His Pro Val Arg Gln Leu Glu Asp Val Asn Leu Leu Asp Gln Met

Ser Lys Gly Arg Phe Arg Phe Gly Ile Cys Arg Gly Leu Tyr Asn Lys

Asp Phe Arg Val Phe Gly Thr Asp Met Asn Asn Ser Arg Ala Leu Ala

Glu Cys Trp Tyr Gly Leu Ile Lys Asn Gly Met Thr Glu Gly Tyr Met

Glu Ala Asp Asn Glu His Ile Lys Phe His Lys Val Lys Val Asn Pro 150



Ala Ala Tyr Ser Arg Gly Gly Ala Pro Val Tyr Val Val Ala Glu Ser 165

Ala Ser Thr Thr Glu Trp Ala Ala Gln Phe Gly Leu Pro Met Ile Leu

Ser Trp Ile Ile Asn Thr Asn Glu Lys Lys Ala Gln Leu Glu Leu Tyr

Asn Glu Val Ala Gln Glu Tyr Gly His Asp Ile His Asn Ile Asp His

Cys Leu Ser Tyr Ile Thr Ser Val Asp His Asp Ser Ile Lys Ala Lys

Glu Ile Cys Arg Lys Phe Leu Gly His Trp Tyr Asp Ser Tyr Val Asn

Ala Thr Thr Ile Phe Asp Asp Ser Asp Gln Thr Arg Gly Tyr Asp Phe 260 265

Asn Lys Gly Gln Trp Arg Asp Phe Val Leu Lys Gly His Lys Asp Thr

Asn Arg Arg Ile Asp Tyr Ser Tyr Glu Ile Asn Pro Val Gly Thr Pro

Gln Glu Cys Ile Asp Ile Ile Gln Lys Asp Ile Asp Ala Thr Gly Ile

Ser Asn Ile Cys Cys Gly Phe Glu Ala Asn Gly Thr Val Asp Glu Ile

Ile Ala Ser Met Lys Leu Phe Gln Ser Asp Val Met Pro Phe Leu Lys

Glu Lys Gln Arg Ser Leu Leu Tyr

<210>

327 <211>

PRT <213> Photorhabdus luminescens <212>

Met Lys Phe Gly Leu Phe Phe Leu Asn Phe Ile Asn Ser Thr Thr Val

Gln Glu Gln Ser Ile Val Arg Met Gln Glu Ile Thr Glu Tyr Val Asp

Lys Leu Asn Phe Glu Gln Ile Leu Val Tyr Glu Asn His Phe Ser Asp

Asn Gly Val Val Gly Ala Pro Leu Thr Val Ser Gly Phe Leu Leu Gly

Leu Thr Glu Lys Ile Lys Ile Gly Ser Leu Asn His Ile Ile Thr Thr 75 80

His His Pro Val Ala Ile Ala Glu Glu Ala Cys Leu Leu Asp Gln Leu



Ser Glu Gly Arg Phe Ile Leu Gly Phe Ser Asp Cys Glu Lys Lys Asp Glu Met His Phe Phe Asn Arg Pro Val Glu Tyr Gln Gln Leu Phe

Glu Glu Cys Tyr Glu Ile Ile Asn Asp Ala Leu Thr Thr Gly Tyr Cys

Asn Pro Asp Asn Asp Phe Tyr Ser Phe Pro Lys Ile Ser Val Asn Pro

His Ala Tyr Thr Pro Gly Gly Pro Arg Lys Tyr Val Thr Ala Thr Ser

His His Ile Val Glu Trp Ala Ala Lys Lys Gly Ile Pro Leu Ile Phe 180

Lys Trp Asp Asp Ser Asn Asp Val Arg Tyr Glu Tyr Ala Glu Arg Tyr

Lys Ala Val Ala Asp Lys Tyr Asp Val Asp Leu Ser Glu Ile Asp His

Gln Leu Met Ile Leu Val Asn Tyr Asn Glu Asp Ser Asn Lys Ala Lys 230

Gln Glu Thr Arg Ala Phe Ile Ser Asp Tyr Val Leu Glu Met His Pro

Asn Glu Asn Phe Glu Asn Lys Leu Glu Glu Ile Ile Ala Glu Asn Ala

Val Gly Asn Tyr Thr Glu Cys Ile Thr Ala Ala Lys Leu Ala Ile Glu

Lys Cys Gly Ala Lys Ser Val Leu Leu Ser Phe Glu Pro Met Asn Asp

Leu Met Ser Gln Lys Asn Val Ile Asn Ile Val Asp Asp Asn Ile Lys

Lys Tyr His Met Glu Tyr Thr 325

8 <210>

394 <211>

PRT

<212> <213> Photorhabdus luminescens

Met Lys Gly Ile Lys Glu Tyr Asp Ser Ser Ala Ala Ile Leu Ser Asn

Ile Ile Leu Arg Ser Lys Thr Gly Met Thr Ser Tyr Val Asp Lys Gln

Glu Ile Thr Ala Ser Ser Glu Ile Asp Asp Leu Ile Phe Ser Ser Asp

Pro Leu Val Trp Ser Tyr Asp Glu Gln Glu Lys Ile Arg Lys Lys Leu



Val Leu Asp Ala Phe Arg Asn His Tyr Lys His Cys Arg Glu Tyr Arg 65

His Tyr Cys Gln Ala His Lys Val Asp Asp Asn Ile Thr Glu Ile Asp 90 95

Asp Ile Pro Val Phe Pro Thr Ser Val Phe Lys Phe Thr Arg Leu Leu 105

Thr Ser Gln Glu Asn Glu Ile Glu Ser Trp Phe Thr Ser Ser Gly Thr
125
115

Asn Gly Leu Lys Ser Gln Val Ala Arg Asp Arg Leu Ser Ile Glu Arg 130 135

Leu Leu Gly Ser Val Ser Tyr Gly Met Lys Tyr Val Gly Ser Trp Phe 145 150

Asp His Gln Ile Glu Leu Val Asn Leu Gly Pro Asp Arg Phe Asn Ala 175

His Asn Ile Trp Phe Lys Tyr Val Met Ser Leu Val Glu Leu Leu Tyr 180

Pro Thr Thr Phe Thr Val Thr Glu Glu Arg Ile Asp Phe Val Lys Thr 200 205

Leu Asn Ser Leu Glu Arg Ile Lys Asn Gln Gly Lys Asp Leu Cys Leu 210 220

Ile Gly Ser Pro Tyr Phe Ile Tyr Leu Leu Cys His Tyr Met Lys Asp 235 240

Lys Lys Ile Ser Phe Ser Gly Asp Lys Ser Leu Tyr Ile Ile Thr Gly 255

Gly Gly Trp Lys Ser Tyr Glu Lys Glu Ser Leu Lys Arg Asp Asp Phe 260 265

Asn His Leu Leu Phe Asp Thr Phe Asn Leu Ser Asp Ile Ser Gln Ile 275

Arg Asp Ile Phe Asn Gln Val Glu Leu Asn Thr Cys Phe Phe Glu Asp 290

Glu Met Gln Arg Lys His Val Pro Pro Trp Val Tyr Ala Arg Ala Leu 320

Asp Pro Glu Thr Leu Lys Pro Val Pro Asp Gly Thr Pro Gly Leu Met 335

Ser Tyr Met Asp Ala Ser Ala Thr Ser Tyr Pro Ala Phe Ile Val Thr 340

Asp Asp Val Gly Ile Ile Ser Arg Glu Tyr Gly Lys Tyr Pro Gly Val 365

Leu Val Glu Ile Leu Arg Arg Val Asn Thr Arg Thr Gln Lys Gly Cys 370

Ala Leu Ser Leu Thr Glu Ala Phe Asp Ser 385



```
<210>
       9
       3098
<211>
       DNA
<212>
       vector pASK75
<213>
<220>
       promoter
<221>
       /function= "beta-la promoter" /label= beta-la /citation= ([1])
<222>
<223>
<220>
       CDS
<221>
        (673)..(1530)
        /product= "beta-la" /citation= )[1])
<222>
 <223>
 <220>
        CDS
 <221>
        (1543)..(2163)
        /product= "tetR" /citation= )[1])
 <222>
 <223>
 <220>
        misc_feature
 <221>
         /function= "ORI" /label= ORI /citation= ([1])
 <222>
 <223>
  <220>
         promoter
  <221>
         /function= "p tetA promoter" /citation= ([1])
  <222>
  <223>
         Use of the tetracycline promoter for the tightly regulated production
  <300>
  <301>
  of a murine antibody fragment in Escherichia coli
         Gene
  <303>
          151
  <304>
   <305>
          131-135
  <306>
          1994-12-30
   <307>
   <309>
          \overline{(1)}..\overline{(3098)}
   <313>
   agcttgacct gtgaagtgaa aaatggcgca cattgtgcga cattttttt gtctgccgtt
                                                                            60
   taccgctact gcgtcacgga tctccacgcg ccctgtagcg gcgcattaag cgcggcgggt
                                                                           120
   gtggtggtta cgcgcagcgt gaccgctaca cttgccagcg ccctagcgcc cgctcctttc
                                                                           180
   gctttcttcc cttcctttct cgccacgttc gccggctttc cccgtcaagc tctaaatcgg
                                                                           240
    gggctccctt tagggttccg atttagtgct ttacggcacc tcgaccccaa aaaacttgat
                                                                           300
    tagggtgatg gttcacgtag tgggccatcg ccctgataga cggtttttcg ccctttgacg
                                                                            360
    ttggagtcca cgttctttaa tagtggactc ttgttccaaa ctggaacaac actcaaccct
                                                                            420
    atctcggtct attcttttga tttataaggg attttgccga tttcggccta ttggttaaaa
                                                                            480
    aatgagctga tttaacaaaa atttaacgcg aattttaaca aaatattaac gcttacaatt
     tcaggtggca cttttcgggg aaatgtgcgc ggaaccccta tttgtttatt tttctaaata
                                                                            600
     cattcaaata tgtatccgct catgagacaa taaccctgat aaatgcttca ataatattga
                                                                            660
```



 $\mathcal{P}$ 

									_0							
aaaa	ıggaa	ıga g	t at Me 1	g ag t Se	t at r Il	t ca e Gl	a ca n Hi 5	t tt s Ph	c cg e Ar	t gt g Va	c gc	c ct a Le 10	u II	t cc e Pr	c ttt o Phe	711
ttt Phe	gcg Ala 15	gca Ala	ttt Phe	tgc Cys	ctt Leu	cct Pro 20	gtt Val	ttt Phe	gct Ala	cac His	cca Pro 25	gaa Glu	acg Thr	ctg Leu	gtg Val	759
aaa Lys 30	gta Val	aaa Lys	gat Asp	gct Ala	gaa Glu 35	gat Asp	cag Gln	ttg Leu	ggt Gly	gca Ala 40	cga Arg	gtg Val	ggt Gly	tac Tyr	atc Ile 45	807
gaa Glu	ctg Leu	gat Asp	ctc Leu	aac Asn 50	agc Ser	ggt Gly	aag Lys	atc Ile	ctt Leu 55	gag Glu	agt Ser	ttt Phe	cgc Arg	ccc Pro 60	gaa Glu	855
gaa Glu	cgt Arg	ttt Phe	cca Pro 65	atg Met	atg Met	agc Ser	act Thr	ttt Phe 70	aaa Lys	gtt Val	ctg Leu	cta Leu	tgt Cys 75	ggc Gly	gcg Ala	903
gta Val	tta Leu	tcc Ser 80	cgt Arg	att Ile	gac Asp	gcc Ala	ggg Gly 85	caa Gln	gag Glu	caa Gln	ctc Leu	ggt Gly 90	cgc Arg	cgc Arg	ata Ile	951
cac His	tat Tyr 95	tct Ser	cag Gln	aat Asn	gac Asp	ttg Leu 100	gtt Val	gag Glu	tac Tyr	tca Ser	cca Pro 105	gtc Val	aca Thr	gaa Glu	aag Lys	999
cat His 110	ctt Leu	acg Thr	gat Asp	ggc Gly	atg Met 115	aca Thr	gta Val	aga Arg	gaa Glu	tta Leu 120	tgc Cys	agt Ser	gct Ala	gcc Ala	ata Ile 125	1047
acc Thr	atg Met	agt Ser	gat Asp	aac Asn 130	act Thr	gcg Ala	gcc Ala	aac Asn	tta Leu 135	ctt Leu	ctg Leu	aca Thr	acg Thr	atc Ile 140	gga Gly	1095
gga Gly	ccg Pro	aag Lys	gag Glu 145	cta Leu	acc Thr	gct Ala	ttt Phe	ttg Leu 150	His	aac Asn	atg Met	GJA	gat Asp 155	cat His	gta Val	1143
act Thr	cgc Arg	ctt Leu 160	Asp	cgt Arg	tgg Trp	gaa Glu	ccg Pro 165	Glu	ctg Leu	aat Asn	gaa Glu	gcc Ala 170	тте	cca Pro	aac Asn	1191
gac Asp	gag Glu 175	g cgt Arg	gac Asp	acc Thr	acg Thr	atg Met 180	Pro	gta Val	gca Ala	atg Met	gca Ala 185	l'l'hr	acg Thr	ttg Leu	cgc Arg	1239
aaa Lys 190	Leu	ı tta ı Leu	act Thr	ggc	gaa Glu 195	Leu	. ctt . Leu	act Thr	cta Leu	gct Ala 200	. Ser	cgg Arg	caa Gln	caa Glr	ttg Leu 205	1287
ata Ile	a gad e Asp	tgg Trp	atg Met	gag Glu 210	Ala	gat Asp	aaa Lys	a gtt s Val	gca Ala 215	ı Gly	a cca / Pro	a ctt D Leu	cto Leu	g cgc Arc 220	tcg g Ser	1335
gco Ala	c ctt a Lei	t dag 1 Pro	g get Ala 225	a Gly	tgg Trp	ttt Phe	atte Ile	gct Ala 230	a Asp	aaa Lys	a tct s Sei	gga Gly	a gco y Ala 235	a GTZ	gag Glu	1383
cg† Ar	t ggo g Gl	c tct y Ser 240	Arg	c ggt g Gly	ato / Ile	c att e Ile	gca e Ala 24	a Ala	a cto a Leo	g ggo ı Gl	g cca y Pro	a gat o Asp 250	o Gly	t aaq y Lys	g ccc s Pro	1431



27	
tcc cgt atc gta gtt atc tac acg acg ggg agt cag gca act atg gat Ser Arg Ile Val Val Ile Tyr Thr Thr Gly Ser Gln Ala Thr Met Asp 255 260 265	1479
gaa cga aat aga cag atc gct gag ata ggt gcc tca ctg att aag cat Glu Arg Asn Arg Gln Ile Ala Glu Ile Gly Ala Ser Leu Ile Lys His 280 285	1527
tgg taggaattaa tg atg tct cgt tta gat aaa agt aaa gtg att aac agc  Met Ser Arg Leu Asp Lys Ser Lys Val Ile Asn Ser  Trp 290 295	1578
gca tta gag ctg ctt aat gag gtc gga atc gaa ggt tta aca acc cgt Ala Leu Glu Leu Leu Asn Glu Val Gly Ile Glu Gly Leu Thr Thr Arg 300 305	1626
aaa ctc gcc cag aag cta ggt gta gag cag cct aca ttg tat tgg cat Lys Leu Ala Gln Lys Leu Gly Val Glu Gln Pro Thr Leu Tyr Trp His 320 325	1674
gta aaa aat aag cgg gct ttg ctc gac gcc tta gcc att gag atg tta Val Lys Asn Lys Arg Ala Leu Leu Asp Ala Leu Ala Ile Glu Met Leu 345	1722
gat agg cac cat act cac ttt tgc cct tta gaa ggg gaa agc tgg caa Asp Arg His His Thr His Phe Cys Pro Leu Glu Gly Glu Ser Trp Gln 350	1770
gat ttt tta cgt aat aac gct aaa agt ttt aga tgt gct tta cta agt Asp Phe Leu Arg Asn Asn Ala Lys Ser Phe Arg Cys Ala Leu Leu Ser 370	1818
cat cgc gat gga gca aaa gta cat tta ggt aca cgg cct aca gaa aaa Cat cgc gat gga gca aaa gta cat tta ggt aca cgg cct aca gaa aaa His Arg Asp Gly Ala Lys Val His Leu Gly Thr Arg Pro Thr Glu Lys	1866
cag tat gaa act ctc gaa aat caa tta gcc ttt tta tgc caa caa ggt Gln Tyr Glu Thr Leu Glu Asn Gln Leu Ala Phe Leu Cys Gln Gln Gly 400 405	1914
ttt tca cta gag aat gca tta tat gca ctc agc gca gtg ggg cat ttt  ttt tca cta gag aat gca tta tat gca ctc agc gca gtg ggg cat ttt  ttt tca cta gag aat gca tta tat gca ctc agc gca gtg ggg cat ttt  ttt tca cta gag aat gca tta tat gca ctc agc gca gtg ggg cat ttt  ttt tca cta gag aat gca tta tat gca ctc agc gca gtg ggg cat ttt  415	1962
act tta ggt tgc gta ttg gaa gat caa gag cat caa gtc gct aaa gaa Thr Leu Gly Cys Val Leu Glu Asp Gln Glu His Gln Val Ala Lys Glu 430 435	2010
gaa agg gaa aca cct act act gat agt atg ccg cca tta tta cga caa Glu Arg Glu Thr Pro Thr Thr Asp Ser Met Pro Pro Leu Leu Arg Gln 455	2058
gct atc gaa tta ttt gat cac caa ggt gca gag cca gcc ttc tta ttc Ala Ile Glu Leu Phe Asp His Gln Gly Ala Glu Pro Ala Phe Leu Phe	2106
ggc ctt gaa ttg atc ata tgc gga tta gaa aaa caa ctt aaa tgt gaa Gly Leu Glu Leu Ile Ile Cys Gly Leu Glu Lys Gln Leu Lys Cys Glu	2154
agt ggg tot taaaagcago ataacctttt toogtgatgg taacttoact Ser Gly Ser	2203



. . .

agtttaaaag gatctaggtg aagatccttt ttgataatct catgaccaaa atcccttaac 2263 gtgagttttc gttccactga gcgtcagacc ccgtagaaaa gatcaaagga tcttcttgag 2323 atccttttt tctgcgcgta atctgctgct tgcaaacaaa aaaaccaccg ctaccagcgg 2383 tggtttgttt gccggatcaa gagctaccaa ctctttttcc gaaggtaact ggcttcagca 2443 gagcgcagat accaaatact gtccttctag tgtagccgta gttaggccac cacttcaaga 2503 actctgtagc accgcctaca tacctcgctc tgctaatcct gttaccagtg gctgctgcca 2563 gtggcgataa gtcgtgtctt accgggttgg actcaagacg atagttaccg gataaggcgc 2623 agcggtcggg ctgaacgggg ggttcgtgca cacagcccag cttggagcga acgacctaca 2683 ccgaactgag atacctacag cgtgagctat gagaaagcgc cacgcttccc gaagggagaa 2743 aggeggaeag gtateeggta ageggeaggg teggaaeagg agagegeaeg agggagette 2803 cagggggaaa cgcctggtat ctttatagtc ctgtcgggtt tcgccacctc tgacttgagc 2863 gtcgattttt gtgatgctcg tcaggggggc ggagcctatg gaaaaacgcc agcaacgcgg 2923 cctttttacg gttcctggcc ttttgctggc cttttgctca catgacccga caccatcgaa 2983 tggccagatg attaattcct aatttttgtt gacactctat cattgataga gttattttac 3043 cactccctat cagtgataga gaaaagtgaa atgaatagtt cgacaaaaat ctaga 3098

10 <210>

286 <211>

<212> PRT vector pASK75 <213>

Met Ser Ile Gln His Phe Arg Val Ala Leu Ile Pro Phe Phe Ala Ala

Phe Cys Leu Pro Val Phe Ala His Pro Glu Thr Leu Val Lys Val Lys

Asp Ala Glu Asp Gln Leu Gly Ala Arg Val Gly Tyr Ile Glu Leu Asp

Leu Asn Ser Gly Lys Ile Leu Glu Ser Phe Arg Pro Glu Glu Arg Phe

Pro Met Met Ser Thr Phe Lys Val Leu Leu Cys Gly Ala Val Leu Ser 75 80

Arg Ile Asp Ala Gly Gln Glu Gln Leu Gly Arg Arg Ile His Tyr Ser

Gln Asn Asp Leu Val Glu Tyr Ser Pro Val Thr Glu Lys His Leu Thr

Asp Gly Met Thr Val Arg Glu Leu Cys Ser Ala Ala Ile Thr Met Ser

Asp Asn Thr Ala Ala Asn Leu Leu Leu Thr Thr Ile Gly Gly Pro Lys 130

٤.

Glu Leu Thr Ala Phe Leu His Asn Met Gly Asp His Val Thr Arg Leu

Asp Arg Trp Glu Pro Glu Leu Asn Glu Ala Ile Pro Asn Asp Glu Arg 170 165

Asp Thr Thr Met Pro Val Ala Met Ala Thr Thr Leu Arg Lys Leu Leu

Thr Gly Glu Leu Leu Thr Leu Ala Ser Arg Gln Gln Leu Ile Asp Trp 200

Met Glu Ala Asp Lys Val Ala Gly Pro Leu Leu Arg Ser Ala Leu Pro

Ala Gly Trp Phe Ile Ala Asp Lys Ser Gly Ala Gly Glu Arg Gly Ser 225

Arg Gly Ile Ile Ala Ala Leu Gly Pro Asp Gly Lys Pro Ser Arg Ile 245

Val Val Ile Tyr Thr Thr Gly Ser Gln Ala Thr Met Asp Glu Arg Asn 265

Arg Gln Ile Ala Glu Ile Gly Ala Ser Leu Ile Lys His Trp 280

<210> 11

<211> 207

<212> PRT

<213> vector pASK75

Met Ser Arg Leu Asp Lys Ser Lys Val Ile Asn Ser Ala Leu Glu Leu

Leu Asn Glu Val Gly Ile Glu Gly Leu Thr Thr Arg Lys Leu Ala Gln

Lys Leu Gly Val Glu Gln Pro Thr Leu Tyr Trp His Val Lys Asn Lys 40

Arg Ala Leu Leu Asp Ala Leu Ala Ile Glu Met Leu Asp Arg His His

Thr His Phe Cys Pro Leu Glu Gly Glu Ser Trp Gln Asp Phe Leu Arg

Asn Asn Ala Lys Ser Phe Arg Cys Ala Leu Leu Ser His Arg Asp Gly

Ala Lys Val His Leu Gly Thr Arg Pro Thr Glu Lys Gln Tyr Glu Thr

Leu Glu Asn Gln Leu Ala Phe Leu Cys Gln Gln Gly Phe Ser Leu Glu

Asn Ala Leu Tyr Ala Leu Ser Ala Val Gly His Phe Thr Leu Gly Cys 135

Val Leu Glu Asp Gln Glu His Gln Val Ala Lys Glu Glu Arg Glu Thr 150



8

Pro Thr Thr Asp Ser Met Pro Pro Leu Leu Arg Gln Ala Ile Glu Leu 175

Phe Asp His Gln Gly Ala Glu Pro Ala Phe Leu Phe Gly Leu Glu Leu 180

Ile Ile Cys Gly Leu Glu Lys Gln Leu Lys Cys Glu Ser Gly Ser 195